

Knots in DNA, proteins and polymers - a tangled challenge

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Ever since Kelvin has conjectured that atoms are composed of knots in the ether, these peculiar objects have stimulated the imagination of mathematicians and natural scientists alike. In recent years the field went through a renaissance and progressed considerably, spurred by the discovery of knotted DNA and proteins.

To set the stage I will discuss the occurrence of knots as measure of entanglement in various polymer models ranging from random walks to worm-like chains to chains with excluded volume interactions before focusing on knots in biopolymers, in particular proteins [1] and DNA.

From an evolutionary point of view protein knots occur in all kingdoms of life and topology is typically preserved amongst homologs. Nowadays, knotted protein structures can even be created artificially, and knotted designs could be used in the future in the context of protein engineering. I will also demonstrate why the folding of knotted proteins may not be so difficult after all by explaining coarse-grained folding simulations of a rather complicated protein, which features six elementary crossings in a projection onto a plane [2]. While knots in globular homopolymers are abundant, protein knots are rare and occur in less than one percent of all known structures. To address this conundrum I will present simulations of a coarse-grained heteropolymer model and argue that the addition of sequence may facilitate evolution towards unknotted proteins even though on average globular heteropolymers are just as knotted as homopolymers.

In the second part I will discuss the occurrence and implications of knots in DNA. Viral DNA is known to be highly knotted in the capsid and shows a preference towards torus-type knots. These phenomena will be explained in the context of coarse-grained simulations of single semiflexible polymers in spherical confinement [3]. I will also present a mechanism, which allows two knots on a polymer chain to pass through each other and swap positions along the strand. Associated "topological" free energy barriers only amount to a few kT, which may enable the interchange of knots on a single DNA molecule [4]. This peculiar mechanism is not only interesting from an aesthetic point of view, but may also play a role in future technological applications such as nanopore sequencing once strand sizes exceed 100000 base pairs.

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[3] D. Reith, P. Cifra, A. Stasiak, P. Virnau, *Nucl. Acids Res.* 40, 5129 (2012).

[4] B. Trefz, J. Siebert, P. Virnau, *PNAS* 111, 7948 (2014).